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EXAMINER

KUBELIK, ANNE R

ART UNIT PAPER NUMBER

1638

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/617,978

Applicant(s)

HERRMANN ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2005 and 20 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 11-31, 38-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 13-19, 21-27, 29-31, 38, 40 and 42 is/are rejected.
- 7) ☒ Claim(s) 11, 12, 20, 39 and 41 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☒ Other: Search notes.

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DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-7 and 11-31) and SEQ ID NO:17 in the reply filed on 27 June 2005 and of nucleic acids encoding SEQ ID NO:20, which includes SEQ ID NOs: 14 and 17, in the reply filed on 20 July 2005 is acknowledged. Applicant has cancelled all claims to non-elected groups, and all arguments are drawn to whether SEQ ID NOs:14 and 17 should be examined together. Applicant was informed in the interview on 20 July 2005 that the initial election was already being treated as an election of nucleic acids encoding SEQ ID NO:20, and if that was novel, that both SEQ ID NOs: 14 and 17 would be examined.

The restriction requirement among the groups and nucleic acids encoding different proteins is still deemed proper and is therefore made FINAL.

2. The abstract is not descriptive of the instant invention, which is a nucleic acid encoding a pesticidal protein from *Androctonus amoreuxi*, plants comprising it, and a method of using it to increase plant pest resistance. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

3. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

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Claim Objections

4. Claims 7, 11 and 19 are objected to because of the following informalities:

Claim 7 has an improper article before "isolated".

Claim 11 has an improper article before "amino" in line 1.

Claim 19 does not start with an article.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 13-19, 21-27, 29-38, 40 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A full review of the specification indicates that nucleic acids encoding pesticidal proteins with 80% identity to SEQ ID NO:20, pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 are essential to the operation of the claimed invention.

The claims are drawn to nucleic acids encoding pesticidal proteins with 80% identity to SEQ ID NO:20, pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID

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NO:17 or bases 64-240 of SEQ ID NO:14, nucleic acids encoding proteins of any function comprising 10 contiguous amino acids of SEQ ID NO:20, nucleic acids of any function comprising 30 contiguous nucleotides of bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, or pesticide-encoding nucleic acids that are complementary to any of the above nucleic acids.

The claimed nucleic acids encode proteins with any type of substitution, insertion or deletion relative to SEQ ID NO:20.

The specification does not describe the relevant characteristics or motifs of the claimed nucleic acids, and the structure of proteins comprising 10 contiguous amino acids of SEQ ID NO:20 is only partial.

The implied function for nucleic acids encoding proteins comprising 10 contiguous amino acids of SEQ ID NO:20 or for nucleic acids comprising 30 contiguous nucleotides of bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 is that they, or the proteins they encode are pesticidal (see claim 23). The claimed function of nucleic acids encoding proteins with 80% identity to SEQ ID NO:20 and nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 is that the encoded proteins be pesticidal. The pesticidal function is not specific; even the specification lists 4 pages of different pests (pg 50-53).

The structural features that distinguish pesticidal proteins with 80% identity to SEQ ID NO:20 from other proteins with 80% identity to SEQ ID NO:20 are not described in the specification, and the structural features that distinguish nucleic acids encoding pesticidal

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proteins with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 from other nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14. The structural features that associate structure with activity against a specific pest are not described. The necessary and sufficient structural elements of a protein with pesticidal activity are not described.

All of the claimed nucleic acids are novel, and thus the prior art cannot provide no well-developed field of prior art to describe the full scope of claimed nucleic acids.

The only species described in the specification are bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, both of which encode SEQ ID NO:20.

Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 alone are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described 80% identity to SEQ ID NO:20, pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, nucleic acids encoding proteins of any function comprising 10 contiguous amino acids of SEQ ID NO:20, nucleic acids of any function comprising 30 contiguous nucleotides of bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, or pesticide-encoding nucleic acids that are complementary to any of the above nucleic acids within the full scope of the claims. Because the sequences are not described, the method of using the sequences to alter a plant pest resistance is likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

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Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

7. Claims 1-7, 13-19, 21-27, 29-31, 38, 40 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:20, expression cassettes, host cells, viruses, plants and seeds comprising them, and methods of using them to alter plant pest resistance, does not reasonably provide enablement for nucleic acids encoding pesticidal proteins with 80% identity to SEQ ID NO:20, pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, nucleic acids encoding 10 contiguous amino acids of SEQ ID NO:20, nucleic acids comprising 30 contiguous nucleotides of bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, or pesticide-encoding nucleic acids that are complementary to any of the above nucleic acids, expression cassettes, host cells, viruses, plants and seeds comprising them, and methods of using them to alter plant pest resistance. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to nucleic acids encoding pesticidal proteins with 80% identity to SEQ ID NO:20, pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, nucleic acids encoding 10 contiguous amino acids of SEQ ID NO:20, nucleic acids comprising 30 contiguous nucleotides of bases 73-

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249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14, or pesticide-encoding nucleic acids that are complementary to any of the above nucleic acids. The claims are also drawn to expression cassettes, host cells, viruses, vectors, and plants comprising the nucleic acids, and methods of making the plants.

The instant specification, however, only provides guidance for isolation of proteins from arthropod venom and sequencing of the proteins (examples 1-4), southern corn rootworm and homopteran feeding assays (examples 5-6), construction of baculoviruses and expression of the proteins in insect cells (examples 7-8), construction of plant expression vectors encoding the pesticidal protein operably linked to a secretion signal sequence (examples 9-12), identification of cDNAs encoding neurotoxins from *Centruroides vittatus* and construction of vectors encoding them (examples 13-14); general guidance for transformation of rice, maize, soybean and assay of the plants for insect resistance (examples 15-20). SEQ ID NO:20 is Aam1 from *Androctonus amoreuxi*; SEQ ID NO:14 is a nucleic acid encoding it that uses rice-preferred codons and the sweet potato sporamin signal sequence, while SEQ ID NO:17 is optimized for expression in *Streptomyces coelicolor* and has the BAA signal peptide (paragraph spanning pg 11-12).

The instant specification fails to provide guidance for how to make or where to find nucleic acids encoding pesticidal proteins with 80% identity to SEQ ID NO:20 or pesticide-encoding nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14. The instant specification also fails to provide guidance for how to use nucleic acids encoding 10 contiguous amino acids of SEQ ID NO:20 and nucleic acids comprising 30 contiguous nucleotides of bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14.

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The instant specification fails to provide guidance for how to make or where to find pesticide-encoding nucleic acids that are complementary to any of the above nucleic acids

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:14 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain pesticidal activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making substitutions is not predictable. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the “conservative” substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while “nonconservative” substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the “nonconservative” amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the “conservative” amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding proteins with 80% identity to SEQ ID NO:20. Making all possible single amino acid substitutions in an 58 amino acid long protein like that of SEQ ID NO:20 would

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require making and analyzing 19^{58} nucleic acids; these proteins would have 98.3% identity to SEQ ID NO:20. Because nucleic acids encoding proteins with 80% identity to SEQ ID NO:20 would encode proteins with 5 amino acid substitutions, many more than 19^{58} nucleic acids would need to be made and analyzed. Nucleic acids with 80% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14 would encode proteins with up to 35 amino acid substitutions and having 39.6% identity to SEQ ID NO:20. Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with up to 35 amino acid substitutions that also have pesticidal activity would require undue experimentation.

Given the claim breadth, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

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Claim 19 is indefinite because it is not clear if the seed is transformed because it comprises the expression construct or because it was transformed with some other nucleic acid.

10. Claims 23-31 and 42-43 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The methods are ones of altering plant pest resistance. The only steps, however, are that of transforming a plant cell. The omitted steps are those involved in regenerating a plant from the plant cell.

11. Claims 1-7, 11-31 and 38-43 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding SEQ ID NO:20. The closest prior art is that of Inceoglu et al (2001, Eur. J. Biochem. 268:5407-5413), who teach a nucleic acid that encodes a protein with 60% identity to SEQ ID NO:20, and Herrmann et al (WO200078957) who teach a nucleic acid with 61% identity to bases 73-249 or SEQ ID NO:17 or bases 64-240 of SEQ ID NO:14

12. Claims 11-12, 20, 39 and 41 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. Claims 28 and 43 are would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

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Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

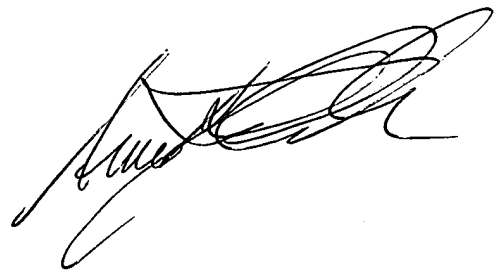
The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Anne R. Kubelik, Ph.D.
September 23, 2005

A handwritten signature in black ink, appearing to read 'Anne R. Kubelik', with a stylized flourish at the end.

**ANNE KUBELIK, PH.D.
PRIMARY EXAMINER**